PATENT
2121-0128P

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of:		Before the Board of Appeals	
Georges BAHR		Appeal No.:	
Appl. No.:	08/809,650	Group:	1648
Filed:	June 13, 1997	Examiner:	L. Scheiner
Conf.:	7849		
For:	COMPOSITIONS OF MURAMYL PEPTIDES INHIBITNIG THE REPLICATION OF HIV		

BRIEF FOR THE APPELLANT UNDER 37 C.F.R. §1.192

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Assistant Commissioner for Patents
Washington, DC 20231

July 18, 2002

Sir:

The due date having been extended for two (2) months to July 18, 2002, the present brief for the Appellant is submitted pursuant to 37 C.F.R. 1.192.

I) Real Party in Interest

The real party in interest in the present application is Vacsyn, S.A. of Paris, France, as evidenced by the assignment recorded at Reel/Frame 8740/0343.

II) **Related Appeals and Interferences**

There are no related appeals or interferences.

III) **Status of Claims**

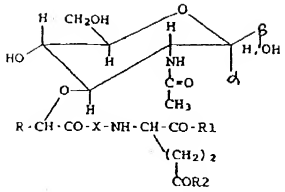
Claims 14-34 were filed with the application and new claims 35-40 were added during prosecution. Claims 14-24 and 35-40 have been cancelled. Thus, claims 25, 26 and 28-34 stand on appeal.

IV) **Status of Amendments**

The amendment filed on February 19, 2002 has been entered. In addition, Appellants have filed an amendment concurrently herewith under 37 C.F.R. 1.116 to cancel non-elected claims 35 and 37-40. The status of the latter amendment is unknown as of the date of the filing of the Appeal Brief.

V) **Summary of Invention**

The present invention is generally directed to "a process for inhibiting the replication of acquired immunedeficiency retroviruses in man or in those animals in which said retroviruses are capable of infecting, which comprises administering as a principle ingredient to said man or said animals in need of such treatment an effective amount of a muramyl peptide of formula:



in which the group R is a methyl group; X is an L-alanyl residue, and R1 is an $O(CH_2)_xH$ group with x=1, 2, 3 or 4, R2 is, independently of R1, either an amino or an $O(CH_2)_xH$ group with x=1, 2, 3, or 4, and wherein said effective amount is also an amount that is capable of causing a 100% inhibition of the replication of said retroviruses in primary cultures of monocytes of the host." (Claim 25).

The specific compounds of the formula described above will be generally referred to, for arguments sake, as the "muramyl peptides of the invention". These compounds constitute a specific sub-class of the muramyl peptides.

It is known that AIDS disease is predominantly caused by the destruction and/or dysfunction of a subpopulation of lymphocytes called helper T cells. However, it has further been shown that the persistence and progression of the infection by the acquired immunodeficiency retroviruses can be attributed to the capacity of specific HIV lines to propagate in monocyte/macrophage line.

Thus, at the early stages of HIV-1 infection, shortly after seroconversion and during the asymptomatic period of AIDS, macrophage tropic or M-tropic strains of the virus predominate, which is in contrast to the late stages of HIV-1 disease in which there is CD4 T cell depletion and progression to AIDS. Thus in the latter stages of AIDS infection T cell lines or T-tropic strains of HIV-1 predominate.

It is thus an object of the present invention to provide a method of inhibiting the replication of acquired immunodeficiency retroviruses, in primary cultures of monocytes of the host by administering as a principal ingredient an effective amount of the specific muramyl peptides of the invention. This effective amount is capable of causing a 100% inhibition of the replication of said retroviruses in primary cultures of monocytes of the host.

In some embodiments (Claims 30-33), the muramyl peptide of the invention is administered together with another molecule capable of enhancing the anti-retroviral action of said muramyl peptide

Prior to Appellants' invention, no one provided such a method for inhibiting the replication of acquired immunodeficiency retroviruses using as the principal ingredient the muramyl peptides of the invention. Appellant's inventive contribution is the demonstration that by administering a particular muramyl peptide to man or animals which are capable of being infected with retroviruses 100% inhibition of the replication of retroviruses in primary cultures of monocytes of the host is achieved. This 100% inhibition was achieved prior to or after retroviral infection. The particular muramyl peptides disclosed in the present application were not known to achieve such a strong inhibition of the retrovirus and were not known prior to the effective filing date of the present invention.

Thus, Appellants are the first to disclose complete inhibition of acquired inmmunodeficiency retroviruses by administration of the defined muramyl peptides of the invention.

VI. Issues

The first issue for appeal is whether the invention of Claims 25, 26, 28 to 30 and 34 satisfies the requirement of novelty, as defined by 35 U.S.C § 102(b), in view of Schreck *et al.*

The second issue for appeal is whether the invention of Claims 25, 26, 28 to 30 and 34 satisfies the requirement of novelty, as defined by 35 U.S.C § 102(b), in view of Masihi *et al.*

The third issue for appeal is whether the invention of Claims 31-33 satisfies the requirement of nonobviousness, as defined by 35 U.S.C § 103(a), in view of Masihi *et al.*

VII. Grouping of Claims

For purposes of appeal, the claims are grouped as follows and will be argued accordingly.

With respect to the appealed ground of rejection for lack of novelty under 35 USC § 102(b) in view of Schreck *et al*, Claims 25, 26, 28 to 30 and 34 do not stand or fall together. Rather, as will be explained below Claims 26 and 28 stand or fall as a separate group.

With respect to the appealed ground of rejection for lack of novelty under 35 USC § 102(b) in view of Masihi *et al*, Claims 25, 26, 28-30, 34 do not stand or fall together. Rather, as will be explained below Claims 26 and 28 stand or fall as a separate group.

With respect to the appealed ground of rejection for lack of nonobviousness under 35 USC § 103(a) in view of Masihi *et al*, Claims 31 to 33 stand or fall together.

VIII. Argument

A. The invention of Claims 25, 26, 28-30, 34 satisfies the requirement of novelty of 35 U.S.C § 102(b), in view of Schreck *et al*.

The Examiner contends that Claims 25, 26, 28-30 and 34 are anticipated by Schreck et al under 35 U.S.C § 102(b). Appellants submit that the rejection cannot be maintained since Schreck et al do not disclose a process for inhibiting the replication of acquired immunodeficiency retroviruses using the muramyl peptides specifically claimed in the present invention.

The Examiner asserts that Schreck et al teach the importance of selecting adjuvants in potential vaccines against AIDS that do not induce activation of the cellular transcription factor nuclear factor-κB (NF-κB) since said (NF-κB) activation has been strongly associated with enhanced replication of human immunodeficiency virus-type 1. More specifically, the Examiner maintains that Schreck *et al*. teach the administration of murabutide, both *in vitro* and *in vivo*, and find that the apyrogenic molecule induced either low activation levels or no activation of (NF-κB).

Throughout the prosecution of the present application, Appellants have asserted that Schreck et al would not be interpreted by the skilled artisan as disclosing that the muramyl peptides can inhibit the replication of immunodeficiency retroviruses. Rather, Schreck et al teach the use of muramyl peptides as adjuvants in AIDS vaccines. Appellants contend that the use of muramyl peptides as adjuvants in vaccines cannot be equated with their role in

inhibiting immunodeficiency retroviruses since there is simply absolutely no disclosure that muramyl peptides can inhibit HIV in Schreck et al.

Furthermore Appellants submit that the Examiner has errored and has not completely identified each and every facet of the claimed process in Schreck et al as required by law in rendering this rejection and expounded upon in *Ex parte Levy*, 17 U.S.P.Q.2d 146 (Bd. Pat. App. & Int'f 1990).

1. Schreck et al falls to disclose that the muramyl peptides disclosed therein can inhibit immunodeficiency retroviruses

Schreck et al. do not teach any specific inhibitory activity on the replication of acquired immunodeficiency retroviruses for any of the muramyl peptides assayed. Indeed throughout the experimental section of this publication no HIV-1 infected cells were used. Rather three types of cells lines were used which were human Jurkat T cells, a human monocyte-macrophage cell line called Mono-Mac-6 and a mouse pre-B cell line 70Z/3.12, which cell lines were not infected with HIV-1, as can be surmised from the Materials and Methods section.

In response to the above argument, the Examiner contends that the method of the invention does not exclude methods of prophylaxis and thus also encompasses treatment of non-infected cells. While Appellants do not disagree with this contention, the Examiner still has not put forth on the record the particular part of Schreck et al that disclose that by administering their disclosed muramyl peptides inhibition of immunodeficiency retroviruses can be achieved.

Indeed, the experiments in Schreck et al only teach the skilled artisan that there is no inducible activation of NF-κB in various cell lines when MDP-(DD), murabutide or MDP(thr)-GDP were tested. It should be born in mind that an absence of activation of NF-κB cannot be equated with inhibition of HIV replication or HIV viral suppression.

The biological definition of inhibition means to decrease, limit or block the action or function of. In the present invention this inhibition concerns immunodeficiency retrovirus replication.

In contrast, activation by biological definition means to convert certain biological compounds into biological derivatives. Thus, in Schreck et al, when the cellular transcription

factor NF-κB is activated, it binds to two motifs in the HIV-1 LTR and consequently activates the LTR-driven RNA transcription, hence increasing HIV-1 replication. When the NF-κB is not activated it remains "dormant" and thus does not lead to an increase in HIV-1 replication.

It was never demonstrated in Schreck et al that any of the muramyl peptides inhibited NF-κB activation and hence might be linked to HIV-1 inhibition.

Furthermore, it is well known that process claims are known to be a means or a method to achieve or produce a result. See, *Corning v. Burden*, 56 U.S. (15 How 267 1853). The result achieved by the presently claimed invention is that of inhibiting the replication of immunodeficiency retroviruses. This result is achieved by administering the muramyl peptides of the present invention.

It cannot be said that Schreck et al demonstrates that the disclosed muramyl peptides possess HIV inhibitory activity.

2. Schreck et al fails to disclose that the muramyl peptides disclosed therein can inhibit immunodeficiency retroviruses

The case law is crystal clear with respect to the requirements that must be met by law to maintain a rejection based on anticipation. Thus, for rejecting any claims under 35 U.S.C. §102 (b), the prior art must disclose each and every element of the challenged claim. See, *Medtronic AVE Inc. v. Cordis Corp.*, 55 USPQ2d 1354 (D.Del 2000).

Moreover, as stated by the Federal Circuit in *Lindeman Maschinefabrik GMBH v. American Hoist and Derrick Co.*, 730 F2d, 1452, 1458 (Fed. Cir. 1984):

> Further, the reference must be sufficiently clear so as to prove the existence of each and every element in the reference.

Appellant's contend that the rejection under 35 U.S.C. § 102(b) cannot be maintained since the major elements of the claims on Appeal are not set forth in this publication neither explicitly nor inherently.

The elements in Claim 25 of record concern the administration of the particular muramyl peptide of the invention as a principal ingredient to inhibit immunodeficiency retroviruses in an effective amount. The effective amount is capable of causing a 100% inhibition of replication of the retrovirus in primary cultures of monocytes of the host.

First of all, Schreck et al fail to disclose administering the muramyl peptides disclosed therein as a principal ingredient. Appellants strongly contend that a principal ingredient cannot be interpreted to mean an adjuvant.

An adjuvant is generally used in conjunction with highly purified subunit vaccines composed of small molecular weight antigens, which were known to be poor immunogens. These subunit vaccines are poor immunogens since they lack, on their critical epitopes, intrinsic adjuvanicity that are usually provided by more complex natural and higher molecular weight molecules. Thus, T cell epitopes which elicit help for antibody production against the B cell epitope reside on the adjuvant portion of the molecule and without such adjuvanicity the antigen produces a lower level of immunity. Furthermore, adjuvants also help to provide the appropriate physical structure to the antigen so that the epitope is identified and processed by the immune system.

Thus, an adjuvant cannot be considered as a principal ingredient in a vaccine, since it is the antigen *per se* that is foremost in importance[1] in a vaccine to obtain immunity and not the adjuvant. It should be emphasized that importance is not a measure of quantity, but effect.

Thus, administering muramyl peptides as a principal ingredient is not disclosed in Schreck et al.

Secondly Schreck et al fails to teach or disclose administering an effective amount of the claimed muramyl peptides of the present invention, wherein said effective amount is also an amount that is capable of causing a 100% inhibition of the replication of said retroviruses in primary cultures of monocytes of the host. This feature is simply not explicitly disclosed in Schreck et al. Nor can it be inherently disclosed since as discussed in Section 1. above, Schreck et al do not disclose that their muramyl peptides can inhibit the replication of immunodeficiency retroviruses.

[1] the definition of principal is foremost in importance

Therefore, Appellants submit that with respect to Claims 25, 28, 29 and 34 Schreck et al cannot be said to explicitly anticipate these claims.

With respect to Claims 26 and 30, Appellants deem that the Examiner was in error by maintaining this rejection. There is no disclosure in Schreck et al of a muramyl peptide of Claim 25 wherein both R1 and R2 are $O(CH_2)_4H$ groups. Likewise for Claim 30 there is simply no disclosure in Schreck et al of administering another compound capable of enhancing the anti-retroviral action of the muramyl peptide with the muramyl compositions of the invention as set forth in Claim 30.

Furthermore, the Examiner's assertion that Schreck et al teach *in vivo* administration of murabutide cannot be found within the four corners of this publication. Rather, Appellant's submit that the reference to muramyl peptides in general is disclosed under the Discussion section with respect to using these muramyl peptides in SIV and HIV vaccines.

Therefore, Appellant's submit that there is no explicit disclosure of Claims 25, 26, 28 to 30 and 34.

Of concern to the Appellant's is that the Examiner has maintained this rejection based on an inherent disclosure. If so, this type of inherency rejection is not clear at all from the record; the Examiner never brought up this issue in any Official Action. Moreover, if this is the case, the Examiner has not met her burden required by law as set forth in *In re Levy, supra*, where the Board of Patent Appeal and Interferences stated the following:

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/ or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the prior art.

Even if the Examiner asserts the inherency principle with respect to anticipation of the claims, although it is not of record, Appellants still maintain that Claims 25, 26, 28 to 30 and 34 are not even inherently anticipated by Schreck et al.

The mere fact that Schreck et al teach in the Discussion section that muramyl peptides have been utilized as adjuvants in experimental vaccines against SIV and HIV does not disclose that these vaccines were capable of inhibiting immunodeficiency retrovirus replication. In fact, the authors only mentioned with respect to these vaccines that they have

"promising activities." What "promising activities" means is certainly not clear and leaves a multitude of doubts.

The Examiner jumps to the erroneous conclusion that the Discussion section in Schreck et al teaches a vaccine in which muramyl peptides were used and hence this vaccine when administered must inhibit immunodeficiency retrovirus replication. This is clearly not explicitly stated and cannot be implicitly implied, since of this date Appellants are not aware of any successful vaccine to treat HIV or SIV. Thus, successful inhibition of an immunodeficiency retrovirus replication has not yet been demonstrated, since a vaccine at the very least would require such inhibition for prophylaxis purposes.

In fact eight (8) years after the publication of Schreck et al, as evidence in Appendix II ("Why don't we have one yet?") there still was no successful HIV vaccine.

To maintain a 35 U.S.C. § 102(b) rejection based on inherent anticipation requires more than assumptions read into the prior art. Rather, there must be a clear disclosure, which is not based on mere promising results. This interpretation is clear as evidenced by the Federal Circuit in *In re Robertson*, 169 F3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) where the Court stated:

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

The fact that Schreck et al disclose that the vaccine using muramyl peptides had promising activities could not lead one to conclude that this vaccine lead to inhibiting the immunodeficiency retrovirus replication. Nor can it be concluded that the effective amounts administered were such that these amounts were capable of causing a 100% inhibition of the replication of said retroviruses in primary cultures of monocytes of the host.

Thus it can only be concluded that Claims 25, 26, 28 to 30 and 34 are not anticipated neither explicitly nor inherently by Schreck et al.

B. The invention of Claims 25, 26, 28-30, 34 satisfies the requirement of novelty of 35 U.S.C § 102(b), in view of Mashi *et al.*

1. **Masihi et al fail to disclose that the murabutide used in the clinical trials as an adjuvant inhibits immunodeficiency r trovirus replication in man and also fails to disclose what effectiv amount should be administered**

The Examiner contends that Masihi *et al.* anticipate Claims 25, 26, 28-30, 34 under 35 U.S.C §102(b). Appellants submit that the rejection is not sustainable.

Appellants also submit that for very similar reasons discussed above in Section A, the Claims are not anticipated by this reference. Appellants deem that equivalent arguments made under the rejection of Schreck et al equally apply to Masihi et al and these arguments are therefore incorporating herein by reference in order to avoid repetitiveness.

The Examiner asserts that since a single sentence in Masihi *et al.* teach that murabutide was used as an adjuvant in human clinical trials for AIDS, that claims 25, 26, 28 to 30 and 34 are anticipated by this reference.

It should be specifically stated that the sole reliance by the Examiner in maintaining this rejection appears at page 397 of Masihi et al where the following is stated:

> A nonpyrogenic butyl ester analog of MDP, murabutide, has been used as an adjuvant in human clinical trials.

First of all it should be stressed that an adjuvant is not considered by those skilled in this art as a principal ingredient. This is not a question of semantics, as the Examiner purports, but a question of scientific terminology. Again, by definition, an adjuvant is a substance which, when used in combination with a specific antigen produces a higher level of immunity than that produced by the antigen alone.

Therefore, an adjuvant cannot be considered as a principal ingredient in a vaccine, since it is the antigen *per se* that is foremost in importance[1] in a vaccine to obtain immunity and not the adjuvant. It should be emphasized that importance is not a measure of quantity, but effect.

[1] the definition of principal is foremost in importance

Moreover, like Schreck et al, Masihi et al is completely silent with respect to the results obtained from the AIDS trial. The mere statement that murabutide has been used does not imply that it has been used with success, such that HIV-1 replication was inhibited. It cannot be assumed from this sole sentence in Masihi et al that inhibition of immunodeficiency retrovirus replication was in fact achieved. A probability that it was, is even insufficient with respect to anticipation by inherency. See, *In re Robertson, supra.*

Thus, since Masihi et al fail to disclose whether the administration of murabutide resulted in inhibition of immunodeficiency retrovirus replication, the effective amounts that could have been administered to achieve this inhibition could not possibly be construed from the four corners of this reference. Masihi et al is thus also silent with respect to the effective amount used is an amount such that 100% inhibition of HIV was obtained in primary cultures of monocytes.

Therefore, each and every element of Claims 25, 28, 29 and 34 are not explicitly nor implicitly disclosed in Masihi et al.

With respect to Claims 26 and 30, Appellants deem, once again, that the Examiner was in error by maintaining this rejection. There is no disclosure in Schreck et al of a muramyl peptide of Claim 25 wherein both R1 and R2 are $O(CH_2)_xH$ groups. Likewise for Claim 30 there is simply no disclosure in Schreck et al of administering another compound capable of enhancing the anti-retroviral action of the muramyl peptide with the muramyl compositions of the invention as set forth in Claim 30.

Therefore, Masihi *et al.* is not prior art under 35 U.S.C. §102(b).

C. The invention of Claims 31-33 satisfies the requirement of nonobviousness, as defined by 35 U.S.C § 103(a), in view of Masihi *et al.*

The Examiner deems that Claims 31-33 are obvious in view of Masihi et al. The Examiner asserts that

> Masihi teach the use of human recombinant GM-CSF in combination with zidovudine for treatment of AIDS in humans and, it would have been obvious to one of ordinary skill in the art at the time of the invention to have administered the murabutide in combination with another molecule such as a cytokine, GM-CSF or a protease inhibitor since said respective molecules are well known to be effective in the treatment of AIDS.

The Examiner has maintained this rejection throughout the following Official Actions.

1. **Masihi et al does not disclose combinations f cytokines or protease inhibitors with an HIV-1 inhibitor**

It should be recalled that Claim 31 and Claim 33 recite that specific molecules such as cytokines and protease inhibitors are used to enhance the retroviral activity of the muramyl peptides. These specific molecules are not disclosed or even suggested within the four corners of Masihi et al. Nor is there any prior art of record that teaches or suggests combining a muramyl peptide with cytokines or protease inhibitors.

As stated in *In re Burt and Walter*, 148 USPQ 549 (CCPA 1966):

> [S]ilence in a reference is not a proper substitute for an adequate disclosure of facts from which a conclusion of obviousness may justifiably follow.

Therefore, Appellants submit that without any disclosure of the combination of cytokines or protease inhibitors with a muramyl peptide as presently claimed, this rejection with respect to Claims 31 and 33 cannot be maintained.

2. **There is no suggestion or motivation to combine a muramyl peptide with GM-CSF in Masihi et al**

When read as a whole Masihi et al discloses that muramyl dipeptide (MDP) has some antiviral activity against HIV infection. The conclusions reached in this publication are clearly set forth in the last paragraph at page 397 which states:

> The rationale for employing agents with the potential to stimulate endogenous CSF production is the possibility they offer for counteracting bone marrow suppression observed in infections and therapy with certain drugs. Muramyl peptides possessing anti-HIV and CSF induction activities may be useful for balancing bone marrow toxicity observed in individuals being treated with dideoxynucleoside analogs like zidovudine. Future studies involving combination of muramyl peptides and dideoxynucleoside analogs are warranted.

Thus, when Masihi et al is read as a whole it suggests to the skilled artisan to use various muramyl peptides in combination with dideoxynucleoside analogs. It does not suggest, as the Examiner maintains to combine muramyl peptides with GM-CSF.

Indeed, it is clear that the Examiner has applied hindsight reconstruction in rendering this rejection, using the Appellant's patent application as a guide knowing that the specification teaches that the claimed muramyl peptides inhibit immunodeficiency retrovirus replication, like zidovudine.

This is forbidden as stated in *In re Pleuddemann*, 910 F2d 823, 828, 15 USPQ2d 1738, 1742 (Fed. Cir. 1990) by the Federal Circuit:

> It is legal error to use "[an inventor's patent]" specification teaching [of both a novel and nonobvious compound and methods of using that compound] as though it were prior art in order to make claims to [the] methods [of use] appear to be obvious.

See also, In *re Gorman*, 933 F2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

However, Masihi et al never suggested combining a muramyl peptide with GM-CSF. Indeed, Masihi et al recognized that although there was some inhibition of HIV-1 using MDP, this inhibition by itself was not sufficient to use MDP alone to treat AIDS. Rather, treatment with a dideoxynucleoside analog was required.

Indeed, the skilled artisan would in fact question this combination, since as stated at page 394 in the paragraph prior to "Materials and Methods" MDP was known to enhance monocyte-macrophage CSF in serum. The skilled artisan knowing this fact would not be motivated to use GM-CSF with a MDP that produces CSF or use a "double dosage" of colony stimulating factor to treat AIDS since Masihi et al clearly indicate the use of muramyl peptide with a dideoxynucleoside analog.

Moreover, there is simply no suggestion or even motivation in Masihi et al to substitute zidovudine with murabutide and then further combine this particular muramyl peptide with GM-CSF, as required by law when the disclosure of a reference requires that some modification be made.

A case very similar to the present issue is that of n *In re Kotzab*, 217 F.3d 1365, 55 USPQ2d 1313 (Fed. Cir. 2000), in which pieces of a sole prior art reference were combined. In this case, the Federal Circuit court stated the following:

> [e]ven when obviousness is based on a single prior art reference, there must be a showing of a suggestion or motivation to modify the teachings of that reference...Moreover, the test for establishing an implicit teaching, motivation or suggestion is what the combination of these two statements of Evans would have suggested to those of ordinary skill in the art, the two statements cannot be viewed in the abstract. Rather, they must be considered in the context of the teaching of the entire reference. Further, a rejection cannot be predicated on the mere identification in Evans of individual components of claimed limitations. Rather, particular findings must be made as to the reason of the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.

It should be apparent that the Examiner has not provided any motivation why the skilled artisan would have selected to substitute zidovudine with murabutide and then further combine this particular muramyl peptide with GM-CSF, especially in view of Masihi et al's teaching that a dideoxynucleoside analog should be present.

Appellants submit that this combination was made by the Examiner through hindsight and with the Appellant's claimed invention clear in her mind. This type of analysis is forbidden by law in maintaining an obviousness rejection.

For these reasons, the Examiner's position is untenable, and Appellant respectfully request reversal of the rejection for obviousness.

D. **Conclusion**

The rejection of Claims 25, 26, 28 to 30 and 34 for anticipation under 35 U.S.C § 102(b), in view of Schreck *et al* is in error. Appellants respectfully request that this rejection be reversed.

The rejection of Claims 25, 26, 28 to 30 and 34 for anticipation under 35 U.S.C § 102(b), in view of Masihi *et al* is in error. Appellants respectfully request that this rejection be reversed.

The rejection of Claims 31-33 for obviousness under 35 U.S.C § 103(a), in view of Masihi *et al* is in error. Appellants respectfully request that this rejection be reversed.

The required Appeal Brief fee in the amount of $160.00 is attached hereto. Appellants further request a two (2) month extension of time for filing the present Appeal Brief. The required extension fee of $200.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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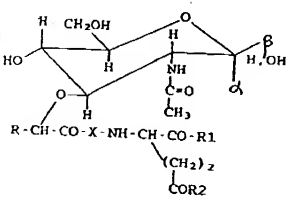
Appendix I-Claims on Appeal

25. A process for inhibiting the replication of acquired immunodeficiency retroviruses in man or in those animals which said retroviruses are capable of infecting, which comprises administering as a principal ingredient to said man or said animals in need of such treatment an effective amount of a muramyl peptide of formula:



in which the group R is a methyl; X is an L-alanyl residue, and R1 is an $O(CH_2)_xH$ group with x= 1, 2, 3 or 4, R2 is, independently of R1, either an amino or an $O(CH_2)_xH$ group with x=1,2,3 or 4, and wherein said effective amount is also an amount that is capable of causing a 100% inhibition of the replication of said retroviruses in primary cultures of monocytes of the host.

25. The process of claim 25, wherein both R1 and R2 are $O(CH_2)_xH$ groups.

28. The process of claim 25, wherein the muramyl peptide is Murabutide.

29. The process of claim 25, which is for the prevention or treatment of AIDS or related syndromes.

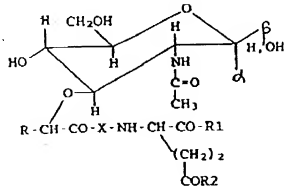
30. The process of claim 25, which comprises administering said muramyl peptide together with another molecule capable of enhancing the anti-retroviral action of said muramyl peptide.

31. The process of claim 30, wherein the other molecule is a cytokine.

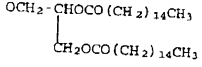
32. The process of claim 30, wherein the other molecule is GM-CSF.

33. The process of claim 30, wherein the other molecule is a protease inhibitor.

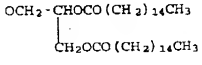
34. The process of claim 25, wherein the muramyl peptide has the formula:



in which the group R is a methyl; X is an L-alanyl residue or L-threonyl residue, and R1 is an O $(CH_2)_xH$ group with x= 1, 2, 3 or 4, R2 is, independently of R1, either an amino or an $O(CH_2)_xH$ group with x=1,2,3 or 4 or a group:



it being understood that, when X is an L-alanyl residue, at least one of these two groups R1 and R2 is an $O(CH_2)_xH$ group as defined above, and that R2 cannot be a group:



and wherein said effective amount is also an amount that is capable of causing a 100% inhibition of the replication of said retrovirus in primary cultures of monocytes of the host.

- The need for an HIV vaccine
- What might a successful vaccine do?
- Why don't we have one yet?
- Vaccine strategies and development
- Preparing for future studies
- Challenges to efficacy studies

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